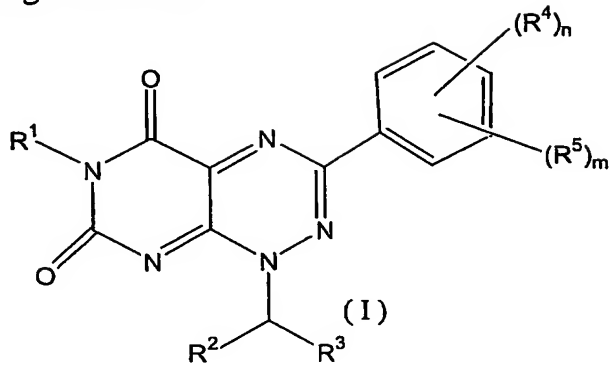
Claims

1. A compound having the formula



(I)

the N-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

n represents an integer being 0, 1 or 2;

m represents an integer being 0 or 1;

R^1 represents hydrogen, Ar^1, C_{1-4}alkyl or C_{1-4}alkyl substituted with morpholinyl or pyridinyl;

R^2 represents hydrogen, phenyl, C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl or C_{1-4}alkyl substituted with hydroxy, phenyl or -oxy-halophenyl;

R^3 represents hydrogen, phenyl, C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl or C_{1-4}alkyl substituted with hydroxy, phenyl or -oxy-halophenyl; or

R^2 and R^3 taken together with the carbon atom to which they are attached form a C_{3-8}cycloalkyl or Het^1 wherein said C_{3-8}cycloalkyl or Het^1 each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from C_{1-4}alkyloxycarbonyl, -C_{1-4}alkyl-Ar^3 C_{1-4}alkylsulfonyl, aminosulfonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl or –C(=NH)-NH_2;

R^4 represents halo, nitro , hydroxy or C_{1-4}alkyloxy;

R^5 represents formyl, hydroxy, cyano, phenyl, -O-Ar^2, NR^6R^7, C_{1-4}alkyl, C_{1-4}alkyloxy, C_{1-4}alkylsulfonyl, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, -O-(mono- or di(C_{1-4}alkyl)aminosulfonyl), Het^2, -SO_2-Het^6, C_{2-6}alkenyl optionally substituted with phenyl,

C_{1-4}alkyl substituted with one or where possible more substituent being selected from hydroxy, halo, Het^3, NR^6R^7 or formyl,

C_{1-4}alkyloxy substituted with one or where possible more substituents being selected from halo, amino, mono- or di(C_{1-4}alkyl)aminosulfonyl, aminosulfonyl, Het^4, NR^8R^9 or -C(=O)-Het^4;

R^6 and R^7 are each independently selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkyloxyC_{1-4}alkyl, Het^5 or C_{1-4}alkyl substituted with one or where possible more substituents being selected from hydroxy, Het^5, C_{1-4}alkyloxycarbonyl, or C_{1-4}alkylsulfonyl;

R^8 and R^9 are each independently selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, Het^7, mono- or di(C_{1-4}alkyl)aminosulphonyl or aminosulphonyl;

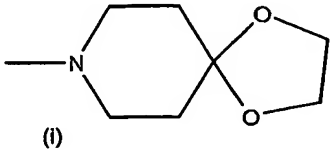
Het^1 represents piperidinyl or dihydroindenyl;

Het^2 represents a heterocycle selected from piperidinyl, morpholinyl, or piperazinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each independently selected from C_{1-4}alkyloxycarbonyl;

Het^3 represents a heterocycle selected from morpholinyl, pyrrolidinyl, pyrrolyl, piperidinyl, or piperazinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each independently selected from hydroxy, C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, hydroxyC_{1-4}alkyl, aminosulfonyl, $NR^{10}R^{11}$, imidazolyl, tetrahydropyrimidinyl, amino, mono- or di(C_{1-4}alkyl)aminosulfonyl, hydroxyC_{1-4}alkyloxyC_{1-4}alkyl, C_{1-4}alkyloxyC_{1-4}alkyl or C_{1-4}alkyloxy;

R^{10} and R^{11} are each independently selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, aminosulfonyl, or mono- or di(C_{1-4}alkyl)aminosulfonyl;

Het^4 represents a heterocycle selected from morpholinyl, piperidinyl, imidazolyl or piperazinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each independently selected from hydroxy, C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, aminosulfonyl or mono- or di(C_{1-4}alkyl)aminosulfonyl or Het^4 represents a monovalent radical represented by formula (i);



(i)

Het^5 represents a heterocycle selected from pyridinyl, pyrimidinyl, pyrrolidinyl, or piperidinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each

independently selected from C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, aminosulfonyl, C_{1-4}alkylaminosulfonyl or mono- or di(C_{1-4}alkyl)aminosulfonyl;

Het^6 represents morpholinyl;

Het^7 represents pyridinyl, piperidinyl, piperazinyl or pyrimidinyl optionally substituted with C_{1-4}alkylphenyl, C_{1-4}alkyloxycarbonyl aminosulfonyl, or mono- or di(C_{1-4}alkyl)aminosulfonyl;

Ar^1 represents an aryl substituent selected from phenyl or naphthalenyl wherein said aryl substituents each independently may optionally be substituted with one, or where possibly two or three substituents each independently selected from nitro or C_{1-4}alkyloxycarbonyl;

Ar^2 represents phenyl optionally substituted with one or where possible two or three substituents each independently selected from the group consisting of halo and nitro;

Ar^3represents an aryl substituent selected from the group consisting of phenyl,

2. A compound according to claim 1 wherein;

R^1 represents Ar^1, C_{1-4}alkyl preferably methyl, or C_{1-4}alkyl substituted with morpholinyl;

R^2 represents hydrogen or C_{1-4}alkyl;

R^3 represents hydrogen or C_{1-4}alkyl; or

R^2 and R^3 taken together with the carbon atom to which they are attached form a C_{3-8}cycloalkyl or Het^1 wherein said C_{3-8}cycloalkyl or Het^1 each independently may optionally be substituted with C_{1-4}alkyloxycarbonyl;

R^4 represents halo preferably chloro or R^4 represents C_{1-4}alkyloxy preferably methoxy;

R^5 represents C_{1-4}alkyloxycarbonyl, -O-(mono- or di(C_{1-4}alkyl)aminosulfonyl), C_{1-4}alkyl substituted with one or where possible more substituent being selected from Het^3 or NR^6R^7,
C_{1-4}alkyloxy substituted with one or where possible more substituents being selected from amino, Het^4 or NR^8R^9;

R^6 and R^7 are each independently selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkyloxyC_{1-4}alkyl, Het^5 or C_{1-4}alkyl substituted with one or where possible more substituents being selected from hydroxy or Het^5;

R^8 and R^9 are each independently selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, Het^7 or mono- or di(C_{1-4}alkyl)aminosulphonyl;

Het^1 represents piperidinyl;

Het^3 represents a heterocycle selected from morpholinyl, pyrrolidinyl, piperidinyl, or piperazinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each independently selected from hydroxy, C_{1-4}alkyl, aminosulfonyl, amino, mono- or di(C_{1-4}alkyl)aminosulfonyl, hydroxyC_{1-4}alkyloxyC_{1-4}alkyl or C_{1-4}alkyloxy;

Het^5 represents pyridinyl optionally substituted with mono- or di(C_{1-4}alkyl)aminosulfonyl;

Het^7 represents piperidinyl optionally substituted with C_{1-4}alkylphenyl, C_{1-4}alkyloxycarbonyl, or mono- or di(C_{1-4}alkyl)aminosulfonyl;

Ar^1 represents an aryl substituent selected from phenyl or naphthalenyl;

3. A compound according to claim 1 wherein;

R^1 represents C_{1-4}alkyl preferably methyl;

R^2 represents C_{1-4}alkyl preferably methyl;

R^3 represents C_{1-4}alkyl preferably methyl; or

R^2 and R^3 taken together with the carbon atom to which they are attached form a C_{3-8}cycloalkyl preferably cyclopentyl or Het^1 preferably piperidinyl wherein said C_{3-8}cycloalkyl or Het^1 each independently may optionally be substituted with C_{1-4}alkyloxycarbonyl preferably t-butoxycarbonyl;

R^4 represents halo or C_{1-4}alkyloxy;

R^5 represents C_{1-4}alkyloxycarbonyl, -O-(mono- or di(C_{1-4}alkyl)aminosulfonyl), C_{1-4}alkyl substituted with one or where possible more substituent being selected from Het^3 or NR^6R^7, C_{1-4}alkyloxy substituted with one or where possible more substituents being selected from amino, Het^4 or NR^8R^9;

R^6 and R^7 are each independently selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkyloxyC_{1-4}alkyl, -Het^5 or C_{1-4}alkyl substituted with one or where possible more substituents being selected from hydroxy, or Het^5;

R^8 and R^9 are each independently selected from hydrogen, C_{1-4}alkyl, -Het^7 or mono- or di(C_{1-4}alkyl)aminosulphonyl;

Het^3 represents a heterocycle selected from piperidinyl, or piperazinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each independently selected from hydroxy, aminosulfonyl, amino, mono- or di(C_{1-4}alkyl)aminosulfonyl, hydroxyC_{1-4}alkyloxyC_{1-4}alkyl or C_{1-4}alkyloxy;

Het^4 represents a heterocycle selected from morpholinyl, piperidinyl or piperazinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each independently selected from C_{1-4}alkyl, C_{1-4}alkyloxycarbonyl or mono- or di(C_{1-4}alkyl)aminosulfonyl;

Het^5 represents a heterocycle selected from pyridinyl or piperidinyl wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible two or three substituents each independently selected from aminosulfonyl, or mono- or di(C_{1-4}alkyl)aminosulfonyl;

Het^7 represents piperidinyl.

4. A compound as claimed in any one of claims 1 to 3 wherein R^2 and R^3 taken together with the carbon atom to which they are attached form a C_{3-8}cycloalkyl, preferably cyclopentyl.

5. A compound according to claim 1 wherein R^5 represents formyl, hydroxy, cyano, phenyl, -O-Ar^2, NR^6R^7, C_{1-4}alkylsulfonyl, C_{1-4}alkylcarbonyl, C_{1-4}alkyloxycarbonyl, -O-(mono- or di(C_{1-4}alkyl)aminosulfonyl), Het^2, -SO_2-Het^6, C_{2-6}alkenyl optionally substituted with phenyl,

C_{1-4}alkyl substituted with one or where possible more substituent being selected from hydroxy, halo, Het^3, NR^6R^7 or formyl, or

C_{1-4}alkyloxy substituted with one or where possible more substituents being selected from halo, amino, mono- or di(C_{1-4}alkyl)aminosulfonyl, aminosulfonyl, Het^4, NR^8R^9 or -C(=O)-Het^4;

6. A compound according to claims 1 or 5 provided that when R^5 represents NR^6R^7, either R^6 or R^7 represents C_{1-4}alkylsulfonyl or C_{1-4}alkylcarbonyl, preferably methylsulfonyl or methylcarbonyl.

7. A compound as claimed in any one of claims 1 to 5 provided that when R^5 represents a C_{1-4}alkyloxy substituted Het^4, said Het^4 being selected from the group consisting of morpholinyl, piperidinyl, piperazinyl and piperazinyl substituted with one C_{1-4}alkyl substituent, preferably methyl, more preferably with the methyl in the para position relative to the carbon atom bearing the R^5 substituent, or Het^4 consists of piperazinyl substituted with one mono- or di(C_{1-4}alkyl)aminosulfonyl substituent, preferably dimethylaminosulfonyl, more preferably with the

dimethylaminosulfonyl in the para position relative to the carbon atom bearing the R^5 substituent.

8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, an effective kinase inhibitory amount of a compound as described in any one of the claims 1 to 7.

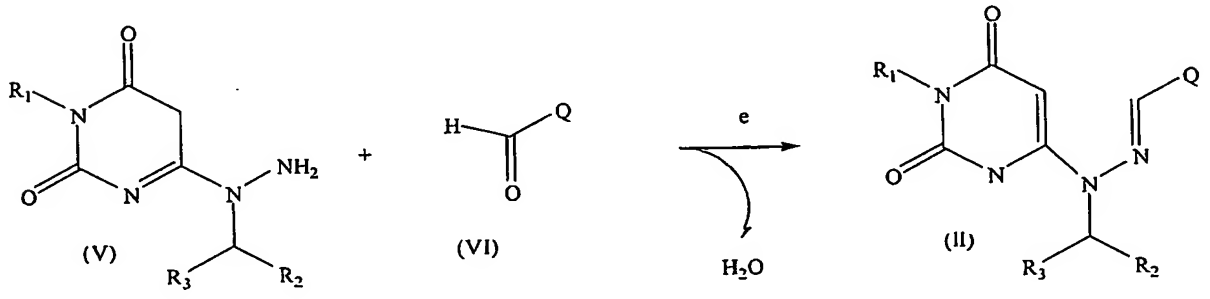
9. A process of preparing a pharmaceutical composition as defined in claim 8, characterized in that, a pharmaceutically acceptable carrier is intimately mixed with an effective kinase inhibitory amount of a compound as described in any one of claims 1 to 7.

10. A compound as claimed in any one of claims 1 to 7 for use as a medicine.

11. Use of a compound as claimed in any one of claims 1 to 7 in the manufacture of a medicament for treating cell proliferative disorders such as atherosclerosis, restinosis and cancer.

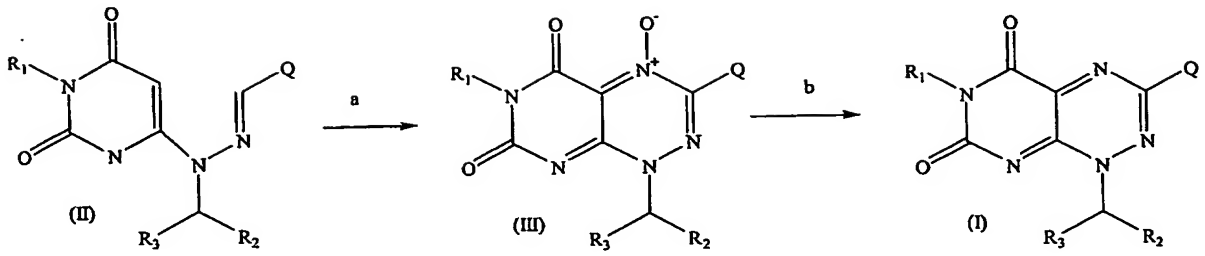
12. A process of preparing a compound as described in claim 1, characterized by

i) reacting a primary amine of formula (V) with an aldehyde of formula (VI) in a condensation reaction using ethanol as a suitable solvent;



e) EtOH

ii) followed by a nitrosative cyclisation of the thus obtained Schiffs bases of formula (II) with $NaNO_2$ in acetic acid, and refluxing the nitroso intermediates of formula (III) in a suitable solvent such as acetic anhydride or ethanol further comprising dithiothreitol (DTT);



a) $NaNO_2$, AcOH, H_2O b) DTT, EtOH